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10/030,390	04/16/2002	Wolfgang Christian Hans	DCKQ:002	2253

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EXAMINER	
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ART UNIT	PAPER NUMBER
1645	12

DATE MAILED: 11/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/030,390	Applicant(s) HANS ET AL.	
	Examiner S. Devi, Ph.D.	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,11 and 19-28* is/are pending in the application.

4a) Of the above claim(s) *28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,11 and 19-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of Applicants' preliminary amendments filed 04/16/02 (paper no.6) and 09/08/03 (paper no. 11). With this, Applicants have amended the specification.

Election

2) Acknowledgment is made of Applicants' election filed 09/08/03 (paper no. 11), of invention IV, claims 10 and 11, in response to the written lack of unity mailed 07/30/03 (paper no. 10).

Status of Claims

3) Claims 11-15 were amended via the preliminary amendment filed 04/16/02.

The non-elected claims 1-9 and 12-18 have been canceled via the amendment 09/08/03.

New claims 19-28 have been added via the amendment 09/08/03.

Claim 28 has been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

The elected claims 10 and 11 and new claims 19-27 are under examination. An Action on the Merits for these claims is issued.

Information Disclosure Statement

4) Acknowledgment is made Applicants' Information Disclosure Statement filed 01/04/02 (paper no. 3). The information referred to therein has been considered and a signed copy is attached to this Office Action (paper no. 12).

Sequence Listing

5) Acknowledgment is made of Applicants' submission of CRF and the raw Sequence Listing which have been entered 05/14/02 (paper no. 8).

Drawings

6) The drawings submitted in the instant application are objected to under 37 C.F.R 1.84 because of the reasons set forth by the Draftsperson in the attached Form PTO 948 (paper no. 12). Correction is required. Applicant is asked to note the changes effected 03 May 2001, particularly the changes to the 'Timing of Corrections':

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 C.F.R 1.85; 1097 O.G. 36

New formal drawings must be filed with the changes incorporated therein. The art unit number, application number (including series code) and number of drawing sheets should be written on the reverse side of the drawings. Applicant may delay filing of the new drawings until receipt of the "Notice of Allowability" (PTOL-37 or PTO-37). If delayed, the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability" to avoid extension of time fees. Extensions of time may be obtained under the provisions of 37 C.F.R 1.136(a) for filing the corrected drawings (but not for payment of the issue fee). The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the three month shortened statutory period set in the "Notice of Allowability" (PTO-37). Within that three month period, two weeks should be allowed for review of the new drawings by the Office. If a correction is determined to be unacceptable by the Office, Applicant must arrange to have an acceptable correction re-submitted within the original three month period to avoid the necessity of obtaining an extension of time with extension fees. Therefore, applicant should file corrected drawings as soon as possible.

Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

Priority

7) The instant application is a national stage 371 application of PCT/EP00/06343, filed 07/05/2000 and claims priority to the European application, 99870143.7, filed 07/05/1999. A

certified copy of the foreign priority document (paper no. 2) has been submitted.

Specification - Informalities

8) The instant specification is objected to because:

(i) The use of the trademarks in the instant specification has been noted in this application. For example, see line 13 on page 16: "Triton X-100"; page 18, line 25 and page 10, line 15: "Superdex 75"; and page 10, lines 13, 14 and 21: 'Coomassie Blue'. Although the use of trademarks is permissible in patent applications, the propriety nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification and make necessary changes wherever trademark recitations appear.

(ii) The Figure descriptions, especially for Figures 1, 3, 5 and 7 are incorrect. Individual Figure numbering in the drawings should be amended as follows:

'Figure 1a' on page 1/15 should be referred to as --Figure 1A, 1B and 1C--.

'Figure 1b' on page 2/15 should be referred to as --Figure 2A--.

'Figure 1b contd.' on page 3/15 should be referred to as --Figure 2B--.

'Figure 1c' on page 4/15 should be referred to as --Figure 3A--.

'Figure 1c contd.'on page 5/15 should be referred to as --Figure 3B--.

'Figure 1d' on page 6/15 should be referred to as --Figure 3C--.

'Figure 1d contd.' on page 7/15 should be referred to as --Figure 3D--.

'Figure 1d contd.' on page 8/15 should be referred to as --Figure 3E--.

'Figure 2' should be referred to as --Figure 4--.

'Figure 3' should be referred to as --Figure 5A, 5B and 5C--.

'Figure 4' should be referred to as --Figure 6--.

'Figure 5' should be referred to as --Figure 7A and 7B--.

'Figure 6' should be referred to as --Figure 8--.

'Figure 7 A and B' should be referred to as --Figure 9A and 9B--.

'Figure 8' should be referred to as --Figure 10--.

Individual Figure descriptions in the specification on pages 9 and 10 should be amended accordingly. All references to these Figures in the specification should be amended to reflect these

changes in numbering.

(iii) The instant application is informal in the format or arrangement of the specification. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the Applicants' use.

Content of Specification

(a) Title of the Invention: See 37 C.F.R 1.72(a). The title of the invention should be placed at the top of the first page of the specification. It should be brief but technically accurate and descriptive, preferably from two to seven words.

(b) Cross-References to Related Applications: See 37 C.F.R 1.78 and M.P.E.P § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See M.P.E.P § 310.

(d) Reference to a "Microfiche Appendix": See 37 C.F.R 1.96(c) and M.P.E.P § 608.05. The total number of microfiche and the total number frames should be specified.

(e) Background of the Invention: The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(f) Brief Summary of the Invention: A brief summary or general statement of the invention as set forth in 37 C.F.R 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms

the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(g) Brief Description of the Several Views of the Drawing(s): A reference to and brief description of the drawing(s) as set forth in 37 C.F.R 1.74. The recitation 'Figure Legends' on page 9 of the specification should be replaced with --Brief Description of the Drawings'--.

(h) Detailed Description of the Invention: A description of the preferred embodiment(s) of the invention as required in 37 C.F.R 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. This item may also be titled "Best Mode for Carrying Out the Invention." Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(i) Claim or Claims: See 37 C.F.R 1.75 and M.P.E.P § 608.01(m). The claim or claims must commence on separate sheet. (37 C.F.R 1.52(b)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps.

(j) Abstract of the Disclosure: A brief narrative of the disclosure as a whole in a single paragraph of 250 words or less on a separate sheet following the claims.

(k) Drawings: See 37 C.F.R 1.81, 1.83-1.85, and M.P.E.P § 608.02.

(l) Sequence Listing: See 37 C.F.R 1.821-1.825.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

9) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

10) Claims 10, 11 and 19-27 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant(s) regards as the invention.

(a) Claim 10 is incorrect and/or redundant in the recitation 'a a recombinant micro-organism'.

(b) Claim 20 is vague and indefinite in the recitation 'preferably' because it is unclear what is encompassed in this limitation. Which other microorganisms other than a gram-positive bacterial strain does this limitation include or exclude is unclear.

(c) Claim 25 is confusing and/or incorrect in the recitation 'administration ..... is orally, anally or vaginally'. For clarity, it is suggested that Applicants replace the limitation with -- administration ..... is by oral, anal or vaginal administration--.

(d) Claims 11 and 24 have improper antecedence in the recitation 'the disorders'. Claims 11 and 24 depend from claim 10, which includes the recitation 'disorder', but not 'disorders'.

(c) Claim 25 is vague, indefinite and confusing in the recitation: 'the administration ... is vaginally'. Claim 25 depends from claim 10 which is directed to a method of treatment of 'gastric and/or intestinal diseases and/or disorder'. It is unclear how a gastric or intestinal disease or disorder can be treated by administering the recited product vaginally.

(e) Claims 11 and 19-27, which depend directly or indirectly from claim 10, are also rejected as being indefinite because of the indefiniteness or vagueness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 103

11) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person. having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the

manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

12) Claims 10, 11, 19-21, 23-25 and 27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Podolsky (WO 97/38712 - Applicants' IDS) and Malin *et al.* (*Ann. Nutr. Metabol.* 40: 137-145, 1996) in view of Steidler *et al.* (WO 97/14806 - Applicants' IDS).

It is noted that the recited TEF1 is synonymous with pS2 (see page 2, lines 1 and 2 of the specification).

Podolsky disclosed a method of treating lesions in the alimentary canal of a patient by administering to the patient an intestinal trefoil factor (ITF) polypeptide, a biologically active fragment thereof, or at least one trefoil peptide. The lesions are in the intestine, oesophagus and stomach of a patient suffering from gastritis, digestive disorder, duodenal ulcer, peptide ulcer diseases, inflammatory bowel diseases, non-ulcer dyspepsia and Crohn's disease (see abstract; claims and column 2; pages 6, 7 and 10). The administration of the peptide is by oral, parenteral or rectal administration (see last full paragraph on page 37). The trefoil polypeptide used for treating or inhibiting the formation of lesions is PS2 (i.e., TEF1) or fragments (i.e., peptides) thereof (see claims; page 11; and mid paragraph on page 36) and is produced by recombinant techniques (see pages 11 and 13-15).

Podolsky do not teach the use in their method of a recombinant microorganism, or a Gram positive bacterium, such as, a *Lactobacillus* species, for *in vivo* delivery of a trefoil peptide, such as, pS2 or TEF1.

However, the delivery of a therapeutically significant polypeptide via probiotic *Lactobacteria* was well known in the art at the time of the invention. Steidler *et al.* demonstrated the use of a non-invasive, food grade *Lactobacillus* species for delivering one or more biologically active polypeptide

antigens *in vivo* (see claims on pages 36 and 37; page 8; and page 4). A method of producing such a recombinant bacterium was taught (see Examples). The one or more biologically active polypeptides include a cytokine, such as, IL-6 (see claim 18), which has the capacity to augment host antigen-specific antibody responses *in vivo* to the antigen with which it is co-expressed (see page 5, last paragraph; and page 6). The recombinant *Lactobacterium* can be used to deliver a range of biologically active polypeptides (see last paragraph on page 11). The biologically active polypeptide can be a receptor or antagonist for biologically active polypeptides (see bottom of page 13), or 'any peptide or polypeptide' to which a receptor of the immune system can bind (see page 18). When an antigen and a cytokine are both expressed by the bacterium, and when such a bacterium is administered to an individual, the immune response to the antigen is enhanced (see first full paragraph on page 24). Steidler *et al.* taught the broad applicability for the delivery of polypeptides via *Lactocobcteria* which are able to sustain their biological activity on a mucous membrane for a sufficient length of time to deliver a biologically active dose of recombinant cytokines and thereby augmenting an immune response to a heterologous antigen (see paragraph bridging pages 8 and 9). The *Lactocobacterium* comprises a recombinant vector comprising the polypeptide-encoding sequence under the control of a promoter sequence and a secretory signal sequence (see pages 15 and 16). The administration of the bacterium is by nasal, oral, vaginal or anal route (see first full paragraph on page 25).

Malin *et al.* taught a method of treating Crohn's disease by oral administration of a composition comprising a Gram positive bacterium, *Lactobacillus* GG, to patients with histologically confirmed Crohn's disease involving sites, such as, ileum, colon, stomach or large bowels (see Table 1; 'Patients and Methods'; and abstract).

Given the therapeutic role of pS2 (TEF1) trefoil peptide in intestinal or gastric lesions, including Crohn's disease, as taught by Podolsky, and given the therapeutic effect of *Lactobacillus* GG also in Crohn's disease as taught by Malin *et al.*, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to express Podolsky pS2 (TEF1) trefoil peptide recombinantly in Malin's *Lactobacillus* using Steidler's expression and delivery method to produce the instant invention, with a reasonable expectation of success, because Steidler *et al.* taught that any biologically active peptide or polypeptide antigen can be delivered *in vivo* via *Lactobacillus*.

One of skill in the art would have been motivated to produce the instant invention for the expected benefit of providing Podolsky's pS2 trefoil peptide, having a demonstrated therapeutic effect against Crohn's disease, in Malin's *Lactobacillus* species, which is also demonstrated to have a therapeutic effect against Crohn's disease as taught by Malin *et al.* such that a product with an advantageous additive therapeutic effect against Crohn's disease can be delivered *in vivo*. It was well known and obvious to one of ordinary skill in the art to combine ingredients which have been separately employed for a particular purpose in order to obtain the expected combination of benefits. See *In re Greenfield*, 571 F2d1185, 197 USPQ 227 (CCPA 1978).

13) Claims 10, 11, 19-25 and 27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Podolsky (WO 97/38712 - Applicants' IDS) in view of Le Page *et al.* (WO 93/17117), Wells *et al.* (*Mol. Microbiol.* 8: 1155-1162, June, 1993) (Wells *et al.*, June, 1993), and Wells *et al.* (*Appl. Environ. Microbiol.* 59: 3954-3959, November 1993) (Wells *et al.*, November, 1993).

It is noted that the recited TEF1 is synonymous with pS2 (see page 2, lines 1 and 2 of the specification).

The teachings of Podolsky are explained above which do not teach in their method the use of a recombinant microorganism, or a Gram positive bacterium, such as, a *Lactococcus lactis* to deliver a trefoil peptide, such as, pS2 or TEF1, *in vivo*.

However, the delivery of a therapeutically significant polypeptide via *Lactobacteria* was well known in the art at the time of the invention. Le Page *et al.* demonstrated the use of a food-grade organism, *Lactococcus lactis*, for the recombinant expression and delivery of a variety of heterologous peptides, polypeptides or proteins of diverse origin. The recombinant product in biologically active form is delivered *in vivo* by parenteral, oral, rectal or topical route. The *Lactococcus lactis* comprises a recombinant vector containing the coding sequence of the polypeptide or peptide desired to be expressed and delivered under the control of an inducible promoter sequence and a secretory signal sequence (see abstract; claims; page 4; and paragraph bridging pages 5 and 6). The *Lactococcus lactis* expressing heterologous protein or polypeptide is used in the production of an immune response in an immunized subject (see page 1). It is taught that the use of a non-invasive microorganism to express a range of foreign proteins opens the way to the concurrent delivery of antigens and cytokines which might be used to drive an immune response in a

desired direction (see page 2, first paragraph).

Wells *et al.* (November, 1993) taught the use of a recombinant *Lactococcus lactis* strain for expression of a heterologous protein using appropriate expression-secretion vectors which incorporate different lactococcal secretion leaders and translation initiation sequences, the *lac* promoter and a bacterial signal leader (see abstract; and page 3954).. The expressed protein has prolonged stability in marked contrast to the proteolysis encountered in other Gram-positive expression systems (see page 3958). Wells *et al.* (November, 1993) taught that innocuous lactic acid bacteria could be used for the production of a number of heterologous proteins of high purity (see page 3954, left column). Wells *et al.* (November, 1993) taught the recombinant *Lactococcus* expression system to be a model system for the expression of a substantial amount of a heterologous protein (see title; and abstract).

Wells *et al.* (June, 1993) demonstrated for the first time that a heterologous peptide antigen of medical importance could be successfully expressed in substantial quantities and in a soluble form via the expression system of a food grade bacterium, *Lactococcus lactis* and be presented to the immune system in an immunogenic form (see abstract; and page 1155). Wells *et al.* (June, 1993) taught that the resultant recombinant *Lactococcus lactis* expressing substantial quantities of the heterologous peptide successfully immunized mice against lethal challenge. Wells *et al.* (June, 1993) expressly taught the continuing need in the art to develop safer vaccines and a growing interest in using live recombinant bacteria as vaccine antigen delivery vehicles which may be taken by mouth (see page 1155, left column; and page 1157, right column). Wells *et al.* (June, 1993) taught how to preload the non-commensal bacterium, *Lactococcus lactis*, with an antigen for use as an antigen delivery vector (see page 1155, right column). The recombinant *Lactococcus lactis* contains the heterologous protein gene under the control of a suitable promoter sequence and the expression vector (see page 1155, right column; and page 1157).

Given the therapeutic role of pS2 (TEF1) trefoil peptide in intestinal or gastric lesions, including Crohn's disease, as taught by Podolsky, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to express Podolsky pS2 (TEF1) trefoil peptide recombinantly in Le Page's or Wells' (June or November, 1993) *Lactobacillus lactis* using Wells' (June or November, 1993) or La Page's expression and delivery method to produce the

instant invention, with a reasonable expectation of success, because Wells *et al.* (June, 1993) taught that a heterologous peptide antigen of medical importance could be successfully expressed in substantial quantities and in a soluble form via *Lactococcus lactis* and be presented to the immune system in an immunogenic form; and Wells *et al.* (November, 1993) taught that heterologous proteins of high purity can be expressed in substantial amounts via the model recombinant *Lactococcus lactis* expression system. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of producing Podolsky's pS2 trefoil peptide, which has a demonstrated therapeutic effect against Crohn's disease, in Wells' (June or November, 1993) or La Page's *Lactobacillus lactis* such that a substantial quantity of soluble pS2 can be delivered *in vivo* with cytokines for driving an immune response in a desired direction as taught by La Page *et al.*

Claims 10, 11, 19-25 and 27 are *prima facie* obvious over the prior art of record.

14) Claim 26 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Podolsky (WO 97/38712 - Applicants' IDS) as modified by Malin *et al.* (*Ann. Nutr. Metabol.* 40: 137-145, 1996) and Steidler *et al.* (WO 97/14806 - Applicants' IDS) as applied to claim 10, and further in view of Silk (WO 8203329).

The teachings of Podolsky as modified by Malin *et al.* and Steidler *et al.* are explained above, which do not teach the use of a gastric catheter for the oral administration of their recombinant microorganism.

However, the use of a gastric catheter as an alternative to the oral administration of a therapeutic composition, especially in patients who are incapable of feeding themselves was routine and conventional in the art at the time of the invention. For instance, see the abstract of Silk.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use Silk's gastric catheter to deliver Podolsky's therapeutic composition as modified by Malin *et al.* and Steidler *et al.* to produce the instant invention, with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing an alternative means of oral administration especially in those patients who are incapable of feeding themselves as taught by Silk.

Claim 26 is *prima facie* obvious over the prior art of record.

Objection(s)

15) Claims 10, 19, 20, 25 and 27 are objected to for the following reasons:

(a) Claims 10, 19, 20, 25 and 27 are objected to for the incorrect limitation 'micro-organism'. To be consistent with the use of this term in the art, it is suggested that Applicants replace the limitation with --microorganism--.

(b) In line 2 of claim 27, for clarity, it is suggested that Applicants replace the recitation 'trefoil peptide coding sequence' with --trefoil peptide-coding sequence'--.

Remarks

16) Claims 10, 11 and 19-27 stand rejected.

17) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center receives transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

18) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. The Examiner can normally be reached on Monday to Friday from 7.45 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

November, 2003

S. DEVI, PH.D.
PRIMARY EXAMINER